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Association of Age, Sex, Race, and Geographic Region With Variation of the Ratio of Basal Cell to Cutaneous Squamous Cell Carcinomas in the United States

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IMPORTANCE Defining which populations are affected by basal cell carcinoma (BCC) vs cutaneous squamous cell carcinoma (cSCC) may inform targeted public health strategies. Incidence of BCC and cSCC is not reported to national cancer registries, but claims data for the treatment of BCC and cSCC provide insights into the epidemiology of keratinocyte carcinoma.

OBJECTIVE To define differences in the ratio of BCC to cSCC in adults (age, ≥18 years) in a large database of patients with commercial insurance and Medicare Advantage coverage.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional analysis used deidentified data derived from the Optum Clinformatics Data Mart to perform a retrospective evaluation of a large commercially insured cohort based on treatment claims from January 1, 2012, to December 31, 2016. Patients with a diagnosed and treated BCC or cSCC as determined by codes from the *International Classification of Diseases, Ninth Revision*, *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*, and *Current Procedural Terminology* were included. Data were analyzed from November 30, 2019, to March 20, 2020.

EXPOSURE Diagnosis and treatment of BCC or cSCC.

MAIN OUTCOMES AND MEASURES The ratio of BCC to cSCC based on age, sex, race, and geographic location. Multivariable logistic regression was used to assess how demographics were associated with the odds of a treated keratinocyte carcinoma being a BCC.

RESULTS Among the 985 317 claims for patients included in the analysis (61.59% for men; mean [SD] age, 69.82 [12.58] years), BCCs were 1.69 (95% CI, 1.6899-1.6901) times more likely than cSCCs to be treated in the United States from 2012 to 2016. Basal cell carcinomas were significantly more prevalent than cSCCs in younger patients (18-39 years, 9.63 [95% CI, 9.6088-9.6574] BCCs per cSCC; 40-64 years, 2.92 [95% CI, 2.9171-2.9187] BCCs per cSCC; and ≥65 years, 1.33 [95% CI, 1.3289-1.3291] BCCs per cSCC; $P < .001$). Basal cell carcinomas were significantly more prevalent than cSCCs in women vs men, except in adults 65 years or older (odds ratios [ORs], 0.98 [95% CI, 0.97-0.99] vs 1.67 [95% CI, 1.47-1.88] for those aged 18-39 and 1.15 [95% CI, 1.12-1.19] for those aged 40-64 years; $P < .001$). The difference in BCC:cSCC ratios between men and women diminished with increasing age (OR, 1.67 for 18-39 years, 1.15 for 40-64 years, and 0.98 for 65 years or older). Basal cell carcinoma was more prevalent than cSCC in all races, including Black patients (BCC:SCC ratios, 1.60 for Asian patients, 1.45 for Black patients, 2.00 for Hispanic patients, and 1.69 for White patients of all ages). The BCC:cSCC ratio varied based on geography, with the highest ratio in the West North Central census division (2.12) and the lowest ratio in the South Atlantic census division (1.35).

CONCLUSIONS AND RELEVANCE In the absence of a national registry, claims data can improve our understanding of the epidemiology of keratinocyte carcinomas. In this cross-sectional study, basal cell carcinomas were more common than cSCCs for all demographics, including in Black patients. In populations younger than 40 years, BCCs were 12.6 times more likely for women and 7.2 times more likely for men. These demographic groups may benefit from public health education focused on the presentation and management of BCCs.

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Supplemental content

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Epidemiological studies shape our understanding of cancer etiology and pathogenesis and inform the way we counsel and care for patients. For skin cancer in the United States, there is a sharp contrast between the high-quality data available for melanoma from cancer registries and the lack of such information for keratinocyte carcinomas (KCs). Because registry data do not exist for KCs, our understanding of KC epidemiology in the United States derives from claims data from an age-restricted cohort,[1] from data on female patients only,[2] or from relatively small samples of data from geographically restricted regions within the United States.[2-4]

Varied conclusions on the relative burden imposed by basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) have been drawn from these restricted study populations. According to Medicare claims data in 2012, the number of treated BCCs and cSCCs was nearly equivalent, and a similar conclusion was drawn from an analysis in northern California.[3] However, older data from small studies of geographically restricted populations have demonstrated BCC:cSCC ratios of 9:1.[4] Studies outside the Medicare population have often noted a predominance of BCC in younger patients but with widely varying point estimates of the relative burden of BCC to cSCC.[3-5] Finally, data on KCs in patients with skin of color in the United States are limited, mostly to regional[6,7] or single-center[8-15] data. Importantly, none of these prior analyses have attempted to simultaneously analyze and adjust their estimates for age, sex, and race; and given that they derive from geographically restricted populations, the geographic variation in the BCC:cSCC ratio is poorly understood.

The aim of this study is to provide insight into the epidemiology of KCs in the United States by analyzing a large insurance claims database with similar sex, regional, and racial demographics to the US population. We evaluated the relative burden of procedurally treated BCC to cSCC in the United States and analyzed how this varied according to age, sex, race, and geographic census division. Defining how demographics shift the BCC:cSCC ratio in the United States could inform targeted public health messaging across different demographic groups.

Key Points

Question Does the ratio of basal cell carcinoma (BCC) to cutaneous squamous cell carcinoma (cSCC) differ with age, sex, race, and geographic region in the United States?

Findings In this cross-sectional study including 985 317 insurance claims, BCCs were especially more common than cSCCs in young women; age and sex interacted to modify this risk, with the difference between men and women decreasing in older patients. Ratios of BCC to cSCC of greater than 1.00 were seen in all races, including Black patients.

Meaning Understanding shifts in the BCC:cSCC ratio based on demographics may inform tailored strategies to educate patients and detect and treat keratinocytic skin cancers.

Methods

This study was deemed exempt from approval and informed consent by the institutional review board at the University of Pennsylvania secondary to the retrospective nature of the study and the use of deidentified data. This repeated cross-sectional study examined paid insurance claims for KCs treated in the United States from January 1, 2012, to December 31, 2016. Data were sourced from the Optum Clinformatics Data Mart (CDM). The Optum CDM is a deidentified, Health Insurance Portability and Accountability Act–compliant insurance claims database collected from both affiliated commercial and Medicare Advantage members of a single national insurance provider. The Optum CDM data compare favorably with 2010 US census data in respect to sex, age, race/ethnicity, and geographical representation (eTable 1 in the Supplement). With respect to age, adults 65 years or older represent 14% of claims available in the Optum CDM and constitute approximately 13% of the overall US population.[16] Diagnosis and procedure codes, the year the claim was filed, US geographic census division (Pacific, Mountain, West North Central, West South Central, East North Central, East South Central, New England, Middle Atlantic, and South Atlantic), race/ethnicity (Asian, Black, Hispanic, and White), sex, and year of birth were determined from each claim. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

The inclusion criteria encompassed all claims with a diagnosis of BCC or cSCC (invasive and in situ) by codes 173.X1, 173.X2, and 232.X from the *International Classification of Diseases, Ninth Revision* (*ICD-9*), codes C44.X1, C44.X2, and D04.X from the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*), and treatment codes from *Current Procedural Terminology* (*CPT*). The *CPT* codes for destruction (17260-17268), Mohs micrographic surgery (17311 and 17313), and excision (11600-11646) were included. The exclusion criteria were claims in patients younger than 18 years or of an unknown sex and for more than 1 cutaneous neoplasm at the same time. Therefore, claims with both BCC and cSCC, BCC or cSCC with melanoma (*ICD-9* code 172.X or *ICD-10* codes C43.X and D05.X), BCC or cSCC with unspecified malignant neoplasm of the skin (*ICD-9* code 173.X0 or *ICD-10* code C44.X0), and BCC or cSCC with other specified malignant neoplasm of the skin (*ICD-9* code 173.X9 or *ICD-10* code C44.X9) present were all excluded. The primary outcome was to describe KC ratios by age, sex, race, and geographic census division. Claims were stratified by sex, age, race, and geographic census division. Three age groupings were prespecified before analysis as 18 to 39, 40 to 64, and 65 years or older and were selected to facilitate data comparison across existing studies. The secondary outcome was to statistically evaluate via multivariable logistic regression how odds of a procedurally treated KC being a BCC varied by age, sex, race, and geographic census division, including an interaction term between age and sex after analyzing the stratified primary data.

Table 1. Demographic Characteristics

Characteristic	Claim group[a] All (N = 985 317)	Complete cases (n = 951 026)
No. of patients	485 479	468 114
KC		
BCC	618 516 (62.77)	596 348 (62.71)
cSCC	366 801 (37.23)	354 678 (37.29)
Sex		
Men	606 853 (61.59)	586 811 (61.70)
Women	378 464 (38.41)	364 215 (38.30)
Age, mean (SD), y	69.82 (12.58)	69.80 (12.58)
Age group, y		
18-39	15 105 (1.53)	14 620 (1.54)
40-64	295 888 (30.03)	286 171 (30.09)
≥65	674 324 (68.44)	650 235 (68.37)
Race/ethnicity		
White	887 001 (90.02)	883 446 (92.89)
Black	39 385 (4.00)	39 252 (4.13)
Hispanic	22 233 (2.26)	22 064 (2.32)
Asian	6295 (0.64)	6264 (0.66)
Unknown	30 403 (3.09)	0
US census region		
New England	35 806 (3.63)	34 446 (3.62)
Middle Atlantic	60 979 (6.19)	58 117 (6.11)
South Atlantic	334 638 (33.96)	325 626 (34.24)
East North Central	127 818 (12.97)	122 879 (12.92)
East South Central	38 028 (3.86)	37 374 (3.93)
West North Central	102 489 (10.40)	98 907 (10.40)
West South Central	78 287 (7.95)	76 457 (8.04)
Mountain	124 257 (12.61)	120 567 (12.68)
Pacific	78 992 (8.02)	76 653 (8.06)
Unknown	4023 (0.41)	0

Abbreviations: BCC, basal cell carcinoma; cSCC, cutaneous squamous cell carcinoma; KC, keratinocyte carcinoma.

[a] Unless otherwise indicated, data are expressed as number (percentage) of claims.

Table 2. Ratio of Procedurally Treated BCC to cSCC When Stratified by Age and Sex[a]

Age group	Ratio, mean (95% CI) [range][b]
All	
Total	1.69 (1.6899-1.6901) [1.64-1.72]
Men	1.63 (1.6305-1.6307) [1.59-1.70]
Women	1.78 (1.7814-1.7816) [1.74-1.80]
18-39 y	
Total	9.63 (9.6088-9.6574) [8.10-11.47]
Men	7.22 (7.1914-7.2472) [5.94-8.59]
Women	12.56 (12.5226-12.6112) [10.67-16.78]
40-64 y	
Total	2.92 (2.9171-2.9187) [2.66-3.21]
Men	2.74 (2.7408-2.7428) [2.50-3.03]
Women	3.18 (3.1787-3.1813) [2.89-3.49]
≥65 y	
Total	1.33 (1.3289-1.3291) [1.28-1.37]
Men	1.34 (1.3379-1.3381) [1.29-1.38]
Women	1.31 (1.3128-1.3132) [1.26-1.35]

Abbreviations: BCC, basal cell carcinoma; cSCC, cutaneous squamous cell carcinoma.

[a] The data include all 985 317 claims, including those of patients with unknown race and census division.

[b] Indicates minimum and maximum value across each year from 2012 to 2016.

Data were analyzed from November 30, 2019, to March 20, 2020. Two cohorts were generated for statistical analysis. The main cohort consisted of claims meeting the study's inclusion and exclusion criteria. Descriptive statistics were generated based on claims data available in this cohort. The BCC:cSCC ratios were also calculated from this main cohort. The second cohort contained only claims with complete information for all variables of interest (sex, age, US census division, and ethnicity). This cohort was used for multivariable logistic regression. As previously stated, the logistic regression model included all variables (age, sex, race, and geographic census division) and an interaction term between sex and age. Age was included in the model as a categorical variable according to the age groupings used in the study. Stata, version 16 (StataCorp LLC), was used to extract relevant *ICD-9*, *ICD-10*, and *CPT* codes from the Optum CDM master files and to perform the statistical analysis. Two-sided $P < .05$ calculated using multivariable logistic regression indicated significance.

Results

Cohort

We identified 1 070 319 paid insurance claims for procedurally treated BCCs or cSCCs from 2012 to 2016. Of these claims, 85 002 (7.94%) contained a diagnosis of BCC and cSCC together, BCC or cSCC with melanoma, or BCC or cSCC with unspecified cutaneous malignant neoplasm on the same claim and were excluded from the main cohort, thereby leaving 985 317 claims in 485 479 patients included in this study (606 853 claims for male patients [61.59%] and 378 464 for female patients [38.41%]; mean [SD] patient age, 69.82 [12.58] years). **Table 1** contains demographic information for the KC claims identified.

A total of 618 516 claims (62.77%) were for BCC and 366 801 (37.23%) for cSCC. The overall ratio of procedurally treated BCCs to cSCCs was 1.69 (95% CI, 1.6899-1.6901). Most claims (951 026 [96.52%]) contained complete information and were included in the multivariable regression analysis.

Age and Biological Sex Differences in Ratio of Treated BCCs to cSCCs

For patients aged 18 to 39 years, the mean ratio of BCC to cSCC was 9.63 (95% CI, 9.6088-9.6574); for those aged 40 to 64 years,

Table 3. Mean BCC:cSCC Ratio by Race[a]

Race by age group	Overall	Men	Women
Asian			
18-39 y	5.43	1.69	11.5
40-64 y	2.65	2.51	2.80
≥65 y	1.27	1.34	1.17
All	1.60	1.57	1.65
Black			
18-39 y	12.23	11.97	12.48
40-64 y	2.32	2.13	2.62
≥65 y	1.16	1.17	1.15
All	1.45	1.40	1.53
Hispanic			
18-39 y	5.86	3.76	7.56
40-64 y	3.01	2.48	3.52
≥65 y	1.57	1.51	1.64
All	2.00	1.76	2.29
White			
18-39 y	9.85	7.37	12.75
40-64 y	2.91	2.75	3.17
≥65 y	1.33	1.34	1.31
All	1.69	1.63	1.77

Abbreviations: BCC, basal cell carcinoma; cSCC, cutaneous squamous cell carcinoma.

[a] The data are based on all claims excluding those with patients of unknown race.

2.92 (95% CI, 2.9171-2.9187); and for those 65 years or older, 1.33 (95% CI, 1.3289-1.3291) (**Table 2**). The odds of a KC being a BCC decreased with increasing age in both sexes.

The association between sex and the ratio of procedurally treated BCC to cSCC was modified by age. Women aged 18 to 39 years were more likely than men to have a treated KC be a BCC (ratio, 12.56 vs 7.22; odds ratio [OR], 1.67; 95% CI, 1.47-1.88; $P < .001$), but differences when comparing women with men diminished with increasing age (OR for ≥65 years, 0.98; 95% CI, 0.97-0.99; $P < .001$) (eTable 2 in the Supplement).

Racial Differences in Ratio of Treated BCCs to cSCCs

After excluding claims of unknown race, 92.89% of claims were from White patients (556 716 BCCs and 330 285 cSCCs), 4.13% from Black patients (23 315 BCCs and 16 070 cSCCs), 2.32% from Hispanic patients (14 810 BCCs and 7423 cSCCs), and 0.66% from Asian patients (3876 BCCs and 2419 cSCCs). The highest BCC:cSCC ratios were in White women aged 18 to 39 years, at 12.75, and Black women aged 18 to 39 years, at 12.48. Black adults 65 years or older had the lowest ratios at 1.16 overall, 1.17 for men, and 1.15 for women. In all races, the ratio of BCC:cSCC declined successively in older age groups, with the exception of Asian men (BCC:SCC ratio of 1.69 for Asian males aged 18-39 years vs 2.51 for Asian males aged 40-64 years) (**Table 3**).

Geographical Variation in the Ratio of Treated BCCs to cSCCs

The highest BCC:cSCC ratios were seen in the West North Central (2.12) and East North Central (2.04) census divisions, and the lowest ratios were seen in the East South Central (1.50) and South Atlantic (1.35) census divisions (eTable 3 in the Supplement). This geographical difference was significant ($P < .001$), with adults in the West North Central region 1.6 times more likely to have a treated KC be a BCC than adults in the South Atlantic region (OR, 1.60; 95% CI, 1.54-1.59). In every region, the BCC:cSCC ratio was higher for women than men aged 18 to 39 and 40 to 64 years. In all regions, the BCC:cSCC ratio declined successively in older groups (eTable 3 in the Supplement). The **Figure** depicts the changing BCC:cSCC ratios across the country.

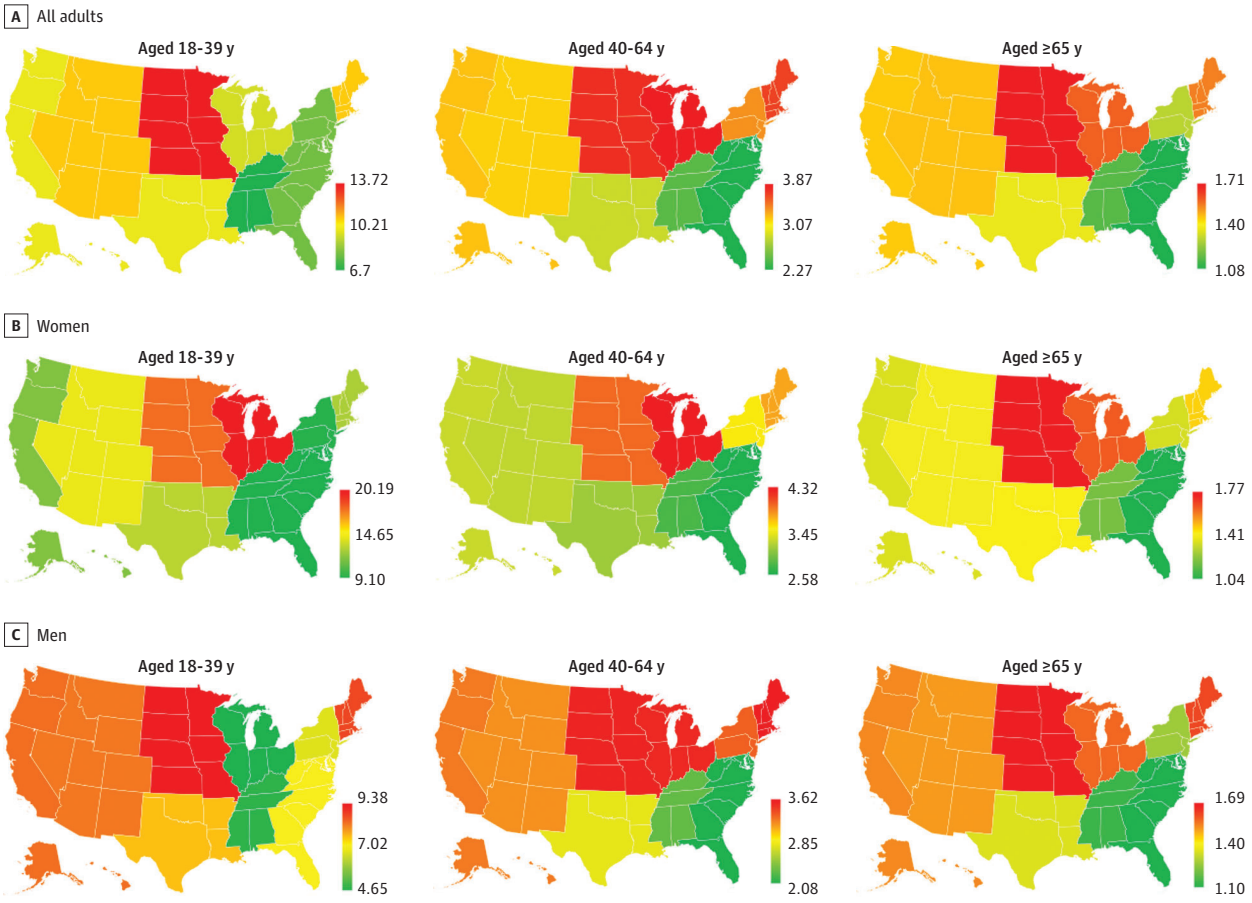
Discussion

The estimated BCC:cSCC ratio in the United States from 2012 to 2016 based on data from a large commercially insured claims database was 1.69. Our analysis expands on prior KC ratio estimates[1-5] and demonstrates how demographics significantly alter the ratio of procedurally treated BCCs to cSCCs. Young women were particularly prone to BCC relative to cSCC, and BCCs were more common than cSCCs, even in Black patients.

The ratio of procedurally treated BCC to cSCC has been noted to vary widely across studies.[1-5] The overall estimated ratio from this study is higher than the 1:1 ratio reported by Rogers et al[1] from 2012 Medicare data. Differences in the populations studied, especially in their age ranges, likely account for the incongruence in the reported ratios between these studies. However, even in the subset of patients 65 years or older, these data indicate a ratio of 1.33, which remains higher than the ratio reported by Rogers et al.[1]

Similar to prior small, geographically restricted studies,[2-4] these data support the assertion that BCC is more likely than cSCC to be a reason for surgery or local tissue destruction in younger populations.[3-5] Basal cell carcinoma was an estimated 9.63 times more common than cSCC in patients aged

Figure. Choropleth Maps of the Mean Ratios of Basal Cell Carcinoma (BCC) to Cutaneous Squamous Cell Carcinoma (cSCC) by US Census Division



The US geographic census divisions include Pacific, Mountain, West North Central, West South Central, East North Central, East South Central, New England, Middle Atlantic, and South Atlantic. Color schemes and scales are not standardized. Each map is scaled to reflect the BCC:cSCC ratios in the representative subgroup. Color bars show ratios.

18 to 39 years. Keratinocyte carcinomas are rare in young adults, but the relative index of suspicion among clinicians for a concerning lesion to be a BCC or cSCC should be adjusted according to the age of the patient, and age-adjusted counseling could be considered when talking to patients about how to self-surveil their skin for KC.

In addition to younger age, female sex was associated with a higher estimated ratio of procedurally treated BCC to cSCC in adults younger than 64 years. The difference between women and men is striking in younger groups. In patients aged 18 to 39 years, the BCC:cSCC ratio was 12.56 in female compared with 7.22 in male patients. In patients 65 years and older, there was a clinically negligible difference of 1.31 in women compared with 1.34 in men in the BCC:cSCC ratio (Table 2). This difference illustrates the significant interaction between age and sex seen in this study.

Why women have a much higher estimated BCC:cSCC ratio than men at younger but not at older ages is an intriguing question. Although this study was not designed to answer this question, a few plausible mechanisms, behavioral and biological, merit mention. From a behavioral perspective, indoor tanning, which is more prevalent in young women, is a possibility.[17,18] Results from a case-control study[19] have shown a significantly increased risk of early-onset (defined as age <40 years) BCC development in those who ever tanned compared with those who never tanned. Second, excess estrogen levels in women, which are especially pronounced in the premenopausal time frame, provide a biologically plausible mechanism for the increased BCC risk in young women that dissipates with age. However, this analysis is speculative, because hormonal effects on KC development in young women are incompletely characterized. Additional research is warranted to properly address declining BCC:cSCC ratios in women as they age.

Basal cell carcinoma was more common than cSCC across all racial subgroups. This is particularly noteworthy in Black patients, in whom prior literature from single-center or regional studies[6,7,20,21] indicated that cSCC was more common than BCC. This finding may reflect selection bias in prior studies or differences between the populations studied in this vs prior reports.

Finally, consistent geographical variations in the ratios of procedurally treated BCC to cSCC were observed. The highest

ratios were identified in the West North Central (2.12) and East North Central (2.04) census divisions, whereas the lowest ratios were found in the East South Central (1.50) and South Atlantic (1.35) census divisions. Higher UV exposure has been reported to increase risk for BCC[2,22] and cSCC[2] in the United States. However, the increased relative risk of KC with higher levels of UV exposure is greater for cSCC (2.05; 95% CI, 1.54-2.73) than for BCC (1.30; 95% CI, 1.18-1.43).[2] The differential effect of UV exposure on cSCC and BCC may partially account for the generally lower BCC:cSCC ratios seen in more southern regions in our data, especially in the southeastern United States (Figure).

Limitations

These findings are not without limitations. The Optum CDM data are collected from patients with private insurance and Medicare Advantage, who likely differ from patients without insurance or with Medicare/Medicaid.[23] How these differences in insurance status could alter the BCC:cSCC ratio is uncertain, but these data are more comprehensive than prior analyses relying on regional[2-4] or Medicare-only[1] populations. Second, subclassifications of BCC (eg, nodular, superficial) and cSCC (eg, invasive vs in situ) were not evaluated. A claims database cannot distinguish between BCC tumor subtypes. Although these data include a small amount of *ICD-10* data (2015q4 and 2016) where in situ and invasive cSCC can be delineated, we did not believe that we could rely on data from the introduction of a new coding system. These data could be considered in future studies. Third, we were unable to confirm KC diagnoses with pathology reports. However, in their regional study evaluating KC incidence in patients younger than 40 years, Christenson et al[5] reported no difference in results when limiting cases to only those confirmed by pathology reports. Fourth, to make our study comparable to prior literature, we did not capture KCs treated with topical medications or with radiotherapy. Inclusion of these cases could alter the ratios seen, but the direction of bias is difficult to estimate because, although the treatment of both superficial BCC and cSCC in situ with topical medications has been described,[24,25] the relative frequency of this practice for BCC and cSCC in situ is unknown. Finally, this study excluded patients with diagnoses of both BCC and cSCC and of BCC or cSCC with melanoma, unspecified malignant neoplasm of the skin, or other specified malignant neoplasm of the skin on the same claim (7.94% of total claims) because treatment could not be definitively attributed to a single diagnosis.

Conclusions

In this cross-sectional study, the estimated ratio of treated BCC to cSCC in the United States, based on data from a large commercially insured claims database, varied across different demographic groups. These data suggest that BCC is especially prevalent relative to cSCC in young women, and this demographic may benefit from public health education focused on the presentation and management of BCCs. In addition, these findings do not support prior literature suggesting that Black patients have higher risk for cSCC than BCC. These data underscore that extrapolating KC epidemiology data derived from age-restricted or regional cohorts can be problematic when generalizing those data to the entire US population.

ARTICLE INFORMATION

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Concept and design: Lukowiak, Aizman, Miller, Higgins, Etzkorn.
Acquisition, analysis, or interpretation of data: Lukowiak, Perz, Sobanko, Shin, Giordano, Higgins, Etzkorn.
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Statistical analysis: Lukowiak, Aizman, Higgins, Etzkorn.
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Supervision: Miller, Sobanko, Giordano, Higgins, Etzkorn.

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Meeting Presentation: An abstract with preliminary data from this project was submitted and accepted for presentation at the Society for Investigative Dermatology 2020 Annual Meeting. The annual meeting was cancelled owing to the coronavirus disease 2019 pandemic, but the abstract was published in the July 2020 installment of the *Journal of Investigative Dermatology*.[26]

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